CLAIMS

1. The use of an anti-angiogenic agent in combination with an inhibitor of the Src family of non-receptor tyrosine kinases in the manufacture of a medicament for use in the substantially normotensive treatment in a warm-blooded mammal such as a human being of a disease state associated with angiogenesis, the Src kinase inhibitor being administered in an amount effective to counteract substantially the hypertension induced by the anti-angiogenic agent.

2. The use of an anti-angiogenic agent in combination with a Src kinase inhibitor according to claim 1 in the manufacture of a medicament for use in the substantially normotensive production of an anti-cancer effect in a warm-blooded mammal such as a human being, the Src kinase inhibitor being administered in an amount effective to counteract substantially the hypertension induced by the anti-angiogenic agent.

3. The use according to claim 1 of an anti-angiogenic agent in combination with a Src kinase inhibitor wherein the anti-angiogenic agent is selected from :-
4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-(pyrrolidin-1-yl)propoxy)quinazoline,
4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-piperidinopropoxy)quinazoline,
4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-((1-methylpiperidin-4-yl)methoxy)quinazoline,
4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-(4-methylpiperazin-1-yl)propoxy)quinazoline,
4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(2-(1-methylpiperidin-4-yl)ethoxy)quinazoline,
4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline,
4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline,
4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(piperidin-4-ylmethoxy)quinazoline,
4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(piperidin-4-ylmethoxy)quinazoline,
4-[(4-fluoro-2-methyl-1*H*-indol-5-yl)oxy]-6-methoxy-7-{3-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]propoxy}quinazoline,
7-{2-[4-(2-fluoroethyl)piperazin-1-yl]ethoxy}-4-[(4-fluoro-2-methyl-1*H*-indol-5-yl)oxy]-6-methoxyquinazoline,

4-[(4-fluoro-2-methylindol-5-yl)oxy]-6-methoxy-7-{3-[4-(2-propynyl)piperazin-1-yl]propoxy}quinazoline,

7-{3-[4-(2-fluoroethyl)piperazin-1-yl]propoxy}-4-[(4-fluoro-2-methyl-1*H*-indol-5-yl)oxy]-6-methoxyquinazoline,

7-(3-(4-acetylpiperazin-1-yl)propoxy)-4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxyquinazoline, and

7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-[(4-fluoro-2-methyl-1*H*-indol-5-yl)oxy]-6-methoxyquinazoline;

or a pharmaceutically-acceptable acid-addition salt thereof.

4. The use according to claim 1 of an anti-angiogenic agent in combination with a Src kinase inhibitor wherein the Src kinase inhibitor selected from :-

4-(2,4-dichloro-5-methoxyanilino)-7-(2-piperidinoethoxy)-5-tetrahydropyran-4-yloxyquinazoline,

4-(2,4-dichloro-5-methoxyanilino)-7-(2-morpholinoethoxy)-5-tetrahydropyran-4-yloxyquinazoline,

4-(6-chloro-2,3-methylenedioxyanilino)-7-(2-pyrrolidin-1-ylethoxy)-5-tetrahydropyran-4-yloxyquinazoline,

4-(6-chloro-2,3-methylenedioxyanilino)-7-(3-pyrrolidin-1-ylpropoxy)-5-tetrahydropyran-4-yloxyquinazoline,

4-(6-chloro-2,3-methylenedioxyanilino)-7-[2-(4-methylpiperazin-1-yl)ethoxy]-5-tetrahydropyran-4-yloxyquinazoline,

4-(6-chloro-2,3-methylenedioxyanilino)-7-(2-piperidinoethoxy)-5-tetrahydropyran-4-yloxyquinazoline,

7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-(6-chloro-2,3-methylenedioxyanilino)-5-isopropoxyquinazoline,

6-methoxy-4-(2,3-methylenedioxyanilino)-7-(3-morpholinopropoxy)quinazoline,

6-methoxy-4-(2,3-methylenedioxyanilino)-7-(3-pyrrolidin-1-ylpropoxy)quinazoline,

6-methoxy-4-(2,3-methylenedioxyanilino)-7-[3-(4-methylpiperazin-1-yl)propoxy]quinazoline,

6-methoxy-4-(2,3-methylenedioxyanilino)-7-(3-piperidinopropoxy)quinazoline,

4-(6-chloro-2,3-methylenedioxyanilino)-7-[3-(4-isobutyrylpiperazin-1-yl)propoxy]-6-methoxyquinazoline,

4-(2-chloro-5-methoxyanilino)-6-methoxy-7-(N-methylpiperidin-4-ylmethoxy)quinazoline,

4-(2-chloro-5-methoxyanilino)-6-methoxy-7-piperidin-4-ylmethoxyquinazoline,
4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-(N-methylpiperidin-4-ylmethoxy)quinazoline,
4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-piperidin-4-ylmethoxyquinazoline,
7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-(5-chloro-2,3-methylenedioxypyrid-4-ylamino)-5-tetrahydropyran-4-yloxyquinazoline,
4-(5-chloro-2,3-methylenedioxypyrid-4-ylamino)-7-{2-[(3RS,4SR)-3,4-methylenedioxypyrrolidin-1-yl)ethoxy]-5-tetrahydropyran-4-yloxyquinazoline,
7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-(5-chloro-2,3-methylenedioxypyrid-4-ylamino)-5-isopropoxyquinazoline and
4-(5-chloro-2,3-methylenedioxypyrid-4-ylamino)-7-{2-[(3RS,4SR)-3,4-methylenedioxypyrrolidin-1-yl)ethoxy]-5-isopropoxyquinazoline;
or a pharmaceutically-acceptable acid-addition salt thereof.

5. A synergistic combination product comprising an anti-angiogenic agent and a Src kinase inhibitor for use simultaneously, sequentially or separately in the production of an anti-cancer effect in a warm-blooded animal such as a human being.

6. A synergistic combination product according to claim 5 wherein the anti-angiogenic agent is selected from the compounds listed in claim 3 and the Src kinase inhibitor is selected from the compounds listed in claim 4.

7. A blood pressure effect sparing combination product comprising an anti-angiogenic agent and a Src kinase inhibitor for use simultaneously, sequentially or separately in the production of an anti-cancer effect in a warm-blooded animal such as a human being.

8. A blood pressure effect sparing combination according to claim 7 wherein the anti-angiogenic agent is selected from the compounds listed in claim 3 and the Src kinase inhibitor is selected from the compounds listed in claim 4.

9. A combination product comprising an anti-angiogenic agent and a Src kinase inhibitor for use simultaneously, sequentially or separately in the production of a substantially normotensive anti-cancer effect in a warm-blooded mammal such as a human being.

10. A combination product according to claim 9 wherein the an anti-angiogenic agent is selected from :-

4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-(pyrrolidin-1-yl)propoxy)quinazoline,

4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-piperidinopropoxy)quinazoline,

4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-(4-methylpiperazin-1-yl)propoxy)quinazoline,

4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(2-(1-methylpiperidin-4-yl)ethoxy)quinazoline,

4-(4-chloro-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline,

4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline,

4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(piperidin-4-ylmethoxy)quinazoline,

4-[(4-fluoro-2-methylindol-5-yl)oxy]-6-methoxy-7-{3-[4-(2-propynyl)piperazin-1-yl]propoxy}quinazoline,

7-(3-(4-acetylpiperazin-1-yl)propoxy)-4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxyquinazoline and

7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxyquinazoline,

or a pharmaceutically-acceptable acid-addition salt thereof;

and the Src kinase inhibitor is selected from :-

4-(6-chloro-2,3-methylenedioxyanilino)-7-(2-pyrrolidin-1-ylethoxy)-5-tetrahydropyran-4-yloxyquinazoline,

4-(6-chloro-2,3-methylenedioxyanilino)-7-(3-pyrrolidin-1-ylpropoxy)-5-tetrahydropyran-4-yloxyquinazoline,

4-(6-chloro-2,3-methylenedioxyanilino)-7-[2-(4-methylpiperazin-1-yl)ethoxy]-5-tetrahydropyran-4-yloxyquinazoline,

4-(6-chloro-2,3-methylenedioxyanilino)-7-(2-piperidinoethoxy)-5-tetrahydropyran-4-yloxyquinazoline,

7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-(6-chloro-2,3-methylenedioxyanilino)-5-isopropoxyquinazoline,

6-methoxy-4-(2,3-methylenedioxyanilino)-7-(3-morpholinopropoxy)quinazoline,

6-methoxy-4-(2,3-methylenedioxyanilino)-7-(3-piperidinopropoxy)quinazoline,

4-(6-chloro-2,3-methylenedioxyanilino)-7-[3-(4-isobutyrylpiperazin-1-yl)propoxy]-6-methoxyquinazoline,

4-(2-chloro-5-methoxyanilino)-6-methoxy-7-(N-methylpiperidin-4-ylmethoxy)quinazoline,

7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-(5-chloro-2,3-methylenedioxypyrid-4-ylamino)-5-tetrahydropyran-4-yloxyquinazoline,

4-(5-chloro-2,3-methylenedioxypyrid-4-ylamino)-7-{2-[(3RS,4SR)-3,4-methylenedioxypyrrolidin-1-yl)ethoxy]-5-tetrahydropyran-4-yloxyquinazoline,

7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-(5-chloro-2,3-methylenedioxypyrid-4-ylamino)-5-isopropoxyquinazoline and

4-(5-chloro-2,3-methylenedioxypyrid-4-ylamino)-7-{2-[(3RS,4SR)-3,4-methylenedioxypyrrolidin-1-yl)ethoxy]-5-isopropoxyquinazoline,

or a pharmaceutically-acceptable acid-addition salt thereof.

11. A pharmaceutical composition comprising a combination product according to any of claims 5 to 10 and a pharmaceutically-acceptable excipient or carrier.

12. A combination product according to any of claims 5 to 10 wherein the anti-angiogenic agent is 4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-piperidinopropoxy)quinazoline, or a pharmaceutically-acceptable acid-addition salt thereof, and the Src kinase inhibitor is 7-[2-(4-acetylpiperazin-1-yl)ethoxy]-4-(6-chloro-2,3-methylenedioxyanilino)-5-isopropoxyquinazoline, or a pharmaceutically-acceptable acid-addition salt thereof.